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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,051	04/03/2006	Giancarlo Tonon	02901/0203976-US0	5959

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EXAMINER	
LONG, SCOTT	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,051	TONON ET AL.	
	Examiner	Art Unit	
	Scott D. Long	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/3/2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claims 15-40 are pending. Claims 15-40 are under current examination.

Sequence Compliance

Sequence Listing and CRF have been received and are acknowledged by examiner. A statement that the Computer Readable Form (CRF) and the Sequence Listing are identical has been submitted and is acknowledged by examiner.

Oath/Declaration

The new oath or declaration, having the signatures of all inventors, received on 3 April 2006 is in compliance with 37 CFR 1.63.

Information Disclosure Statement

The Information Disclosure Statements (IDS) filed on 11 May 2006 consisting of 1 sheet(s) are in compliance with 37 CFR 1.97. Accordingly, examiner has considered the Information Disclosure Statements.

Priority

This application claims benefit as a 371 of PCT/IT04/00529 (filed 09/27/2004). The application claims benefit of foreign application ITALY MI2003A001909 (filed 10/03/2003). The instant application has been granted the benefit date, 3 October 2003, from the application ITALY MI2003A001909.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 15 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 15 and 28 contain the acronym, "CMAH." This is unclear and the specification does not clearly identify this term as meaning, "CMP-N-acetylneuraminic acid hydroxylase." Furthermore, some of the art uses "CNAH" for "CMP-N-acetylneuraminic acid hydroxylase." Therefore, to be clear, the

examiner requests that claims 15 and 28 be amended such that the term "CMP-N-acetylneuraminic acid hydroxylase (CMHA)" is substituted for "CMAH."

Claims 16-25 and 29-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Since all of these claims begin with "a CHO cell," rather than the commonly used and properly dependent form of "the CHO cell of claim 15," it is unclear that the claims are properly dependent. Clarification is required. The objection could be overcome by amending the claims to change the first word of the claims to "The."

Claims 15-25 and 28-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, because a variety of phrases:

Claims 15 and 28 contain the phrase, "a portion of the gene," the metes and bounds of this term are not clear in the specification. Could this "portion" be a full length deletion or only a fraction of the gene? Or might the [deleted] portion be less than full length and yet larger than the sequence disposed between? Clarification is requested.

Claims 17, 30-31, and 33 contain the phrase "is disposed between;" the metes and bounds of these regions are not clear. Does this mean a deletion exactly defined by certain bases or could it mean any of a set of deletions within the broader range?

Claim 18 contains the phrase, "said portion is within encoding for the sequence disposed between bases;" the examiner finds this language confusing and unclear. Is the [deleted] portion within the sequence defined by the bases 787 and 1598 or does

the portion encode an [amino acid] sequence encoded within bases 787 and 1598 of the cDNA? Clarification is requested.

Claim 21 recites the limitation "wherein said portion has the sequence of SEQ ID NO:2," but claim 15 describes "a portion of the gene" (i.e. DNA), while SEQ ID NO:2 is an amino acid sequence. There is insufficient antecedent basis for this limitation in the claim. Clarification is requested.

Claims 26-27 and 39-40 are also rejected under 35 U.S.C. 112, second paragraph, as being indefinite, because the methods require the cells of claims 15 and 28, which are indefinite.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 15-40 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Fontana et al (Animal Cell Technology: Products from Cells, Cells as Products, 245-249. 1999).

Claim 15 is directed to a CHO cell deprived of a portion of the gene encoding for CMAH. According to the specification, CMAH is CMP-NeuAc hydroxylase, which can

be expanded to CMP-N-acetylneuraminic acid hydroxylase. Fontana et al. abbreviate the CMP-N-acetylneuraminic acid hydroxylase gene as CNAH (page 245). Fontana et al. teach homologous recombination of CHO cells using a plasmid comprising DNA sequences coding for biologically active domains of CNAH.

Claim 16 is directed to the CHO cell of claim 15, wherein the cell is deprived of a gene sequence which encodes for the binding site to the substrate (CMP-N-acetylneuraminic acid) and for the binding site to the cofactor (b5 cytochrome). Fontana et al. teach, CHO cells which comprise a knock-out of the coding sequence for cytochrome b5 binding site and of the binding site for CMP-N-acetylneuraminic acid.

Claims 17-22 are describing the deleted portion of the CMAH gene in such a way that it is not possible to compare the prior art to the limitations of the claims. Fontana et al. describe the Hampster CNAH cDNA sequence [with indications of exons and binding domains for CNAH and Cyt b5] and alignment with SEQ IDNO:2 of the instant application indicates that the sequences are the same in the region of the binding domains. The exon identification of the instant application is not the same that of the Fontana et al. reference. However, when SEQ ID NO:1 is translated into polypeptide sequence, it is the same as SEQ ID NO:2. From what the examiner can decipher, it seems that the portions of the CMAH gene which encode binding domains for CMP-N-acetylneuraminic acid and for b5 cytochrome are suggested by Fontana et al. as important for deletion through homologous recombination in CHO cells. The examiner believes these teachings satisfy the limitations of claims 17-22.

Claims 23 is obvious, since Fontana et al. teach "the aim of knocking-out the CNAH gene in CHO cells, for the production of recombinant glycoproteins devoid of NeuGc" because "NeuGc is potentially antigenic in man" (page 245). It would be important to knock-out both alleles to create a cell line that produces recombinant proteins devoid of NeuGc residues.

Claim 24-25 is directed to a CHO cell according to claim 15, wherein the portion elimated has been replaced by at least one DNA sequence encoding for resistance to an antibiotic. Claim 25 further limits the antibiotic of claim 24 to zeocine. Fontana et al. teach "a replacement cassette...carrying the zeocin resistance gene" (page 247).

Claims 26-27 are directed to methods of expressing heterologous recombinant protein in CHO cells of claim 15, wherein said protein is at least one recombinant glycoconjugate. Fontana et al. teaches the goal of their method is "the production of recombinant glycoproteins" (page 245).

Claim 28 is directed to a CHO cell deprived of the portion of the gene encoding the catalytic domain of CMAH. It seems that the deletions taught by Fontana et al. have deleted functional domains of CMAH.

Claim 29 is directed to a CHO cell according to claim 28 deprived of the gene sequence which encodes the binding site to the substrate (CMP-N-acetylneuraminic acid) and the binding site to cofactor (b5 cytochrome). It seems that the deletions taught by Fontana et al. have deleted functional domains of CMAH, including CMP-N-NeuAc binding site and b5 cytochrome binding site.

Claims 30-35 are describing the deleted portion of the CMAH gene in such a way that it is not possible to compare the prior art to the limitations of the claims. Fontana et al. describe the Hampster CNAH cDNA sequence [with indications of exons and binding domains for CNAH and Cyt b5] and alignment with SEQ IDNO:2 of the instant application indicates that the sequences are the same in the region of the binding domains. The exon identification of the instant application is not the same that of the Fontana et al. reference. However, when SEQ ID NO:1 is translated into polypeptide sequence, it is the same as SEQ ID NO:2. From what the examiner can decipher, it seems that the portions of the CMAH gene which encode binding domains for CMP-N-acetylneuraminic acid and for b5 cytochrome are suggested by Fontana et al. as important for deletion through homologous recombination in CHO cells. The examiner believes these teachings satisfy the limitations of claims 30-35.

Claims 36 is obvious, since Fontana et al. teach "the aim of knocking-out the CNAH gene in CHO cells, for the production of recombinant glycoproteins devoid of NeuGc" because "NeuGc is potentially antigenic in man" (page 245). It would be important to knock-out both alleles to create a cell line that produces recombinant proteins devoid of NeuGc residues.

Claim 37-38 is directed to a CHO cell according to claim 28, wherein the portion elimated has been replaced by at least one DNA sequence encoding for resistance to an antibiotic. Claim 38 further limits the antibiotic of claim 37 to zeocine. Fontana et al. teach "a replacement cassette...carrying the zeocin resistance gene" (page 247).

Claims 39-40 are directed to methods of expressing heterologous recombinant protein in CHO cells of claim 28, wherein said protein is at least one recombinant glycoconjugate. Fontana et al. teaches the goal of their method is "the production of recombinant glycoproteins" (page 245).

Accordingly, Fontana et al. anticipated the instant claims.

Conclusion

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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